DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

466 Fernandez Juncos Avenue
Puerta De Tierra
San Juan, Puerto Rico 00901-3223

November 1, 2000

WARNING LETTER
SJN-01-02

CERTIFIED MAIL
Return Receipt Requested

Mr. Raymond Gilmartin
Merck & Co, Inc.
One Merck Drive
P.O. Box 100
Whitehouse Station, NJ 08889-100

Dear Mr. Gilmartin:

From September 18 to October 6, 2000, an investigator from the San Juan District Office of the Food and Drug Administration conducted an inspection of your prescription drug manufacturing facility, Merck, Sharp & Dohme Quimica de Puerto Rico located at Road #2, Km 60.3 Sabana Hoyos, Arecibo, Puerto Rico. Our evaluation of the information obtained during the inspection determined that the pharmaceutical products manufactured by the facility are adulterated within the meaning of section 501(a)(2)(b) of the Federal Food, Drug and Cosmetic Act (the Act) because they were not manufactured in accordance with Good Manufacturing Practice Regulations (GMP) as defined in Title 21, Code of Federal Regulations, Part 211 (21 CFR 211).

The deficiencies found during the inspection, and reported on the List of Inspectional Observations, FDA-483, presented at the conclusion of the inspection include the following:

1. Test results submitted to the FDA investigator during the inspection were false and misleading in that the actual test which reportedly generated the test results recorded in Operations Qualification (OQ) Protocol, AR-Q94-1M-49-A1, for [redacted] Weight Variation System Stations was never performed. According to your own internal investigation, your employees reported test results for which no testing occurred. In addition, the results for testing that was performed, was not accurately reported in that the expected results were recorded rather than the actual results. Furthermore, your management review of the qualification protocol, test results and the final reports failed to prevent or even detect the problem. [21 CFR 211.68 and 21 CFR 211.160(b)(4)]

2. Failure to follow written analytical test methods for Fosamax Tablets. Your firm did not perform the required standard injection bracketing

required for the HPLC method for both assay and content uniformity. [21 CFR 211.165(a)]

We acknowledge receipt of your response letter, dated October 11, 2000, and signed by Ms. Daneris Fernandez. Our evaluation of the response letter finds the response is not adequate to correct the underlying causes of the observations. The corrective action outlined for observation #1 does not address the issue of why your quality system was not able to prevent and/or detect the faulty data in the final qualification report. The fact that multiple members of your management staff reviewed and approved both the original qualification protocol and the final report without detecting the faulty data is not adequately addressed. The corrective action to observation #2 does not address the underlying issue of why your quality system did not detect the fact that your employees were not following the procedure.

The above identification of violations is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure adherence with each requirement of the Good Manufacturing Practice Regulations. Federal agencies are advised of the issuance of all warning letters about drugs so that they may take this information into account when considering the award of contracts.

You should take prompt action to correct these violations, and you should establish procedures whereby such violations do not recur. Failure to promptly correct these violations may result in regulatory sanctions. These sanctions include, but are not limited to, seizure and/or injunction.

Please notify the San Juan District office in writing, within 15 working days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to prevent the recurrence of these or similar violations.

Your reply should be sent to the Food and Drug Administration, San Juan District Office, 466 Fernandez Juncos Ave., San Juan, Puerto Rico, 00901-3223,
Attention: Mary Mason, Compliance Officer.

Sincerely,

Mildred R. Barber
District Director

cc:

Ms. Daneris Fernandez, General Manager
Merck Sharp & Dohme Quimica de Puerto Rico, Inc.
P.O. Box 6060
Barceloneta, PR 00617

Mr. Robert H Boisclaire, Senior Vice President
Operations-The Americas
Merck & Co., Inc.
770 Sunnytown Pike
PO BOX 4, WP-39-412
West Point, PA 19486-0004